# APPROXIMATE SIMULATION OF ACUTE HYPOBARIC HYPOXIA WITH NORMOBARIC HYPOXIA

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**INTRODUCTION.** Some manufacturers of reduced oxygen ($O_2$) breathing devices claim a comparable hypobaric hypoxia (HH) training experience by providing $F_IO_2 < 0.209$ at or near sea level pressure to match the ambient $O_2$ partial pressure (iso-$pO_2$) of the target altitude. **METHODS.** Literature from investigators and manufacturers indicate that these devices may not properly account for the 47 mmHg of water vapor partial pressure that reduces the inspired partial pressure of $O_2$ ($P_IO_2$). Nor do they account for the complex reality of alveolar gas composition as defined by the Alveolar Gas Equation. In essence, by providing iso-$pO_2$ conditions for normobaric hypoxia (NH) as for HH exposures the devices ignore $P_AO_2$ and $P_ACO_2$ as more direct agents to induce signs and symptoms of hypoxia during acute training exposures. **RESULTS.** There is not a sufficient integrated physiological understanding of the determinants of $P_AO_2$ and $P_ACO_2$ under acute NH and HH given the same hypoxic $pO_2$ to claim a device that provides isohypoxia. Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic $pO_2$ is an incomplete hypoxic dose. Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m). **CONCLUSIONS.** At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient $pO_2$ at sea level as at altitude (iso-$pO_2$ machines). An approach to reduce the overestimation is to at least provide machines that create the same $P_IO_2$ (iso-$P_IO_2$ machines) conditions at sea level as at the target altitude, a simple software upgrade.

Learning Objectives:

1. Applying basic principles of respiratory physiology to the design of reduced oxygen breathing devices.
2. Working toward a better understanding of hypoxia.

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## ABSTRACT

INTRODUCTION. Some manufacturers of reduced oxygen ($O_2$) breathing devices claim a comparable hypobaric hypoxia (HH) training experience by providing $F_IO_2$ < 0.209 at or near sea level pressure to match the ambient $O_2$ partial pressure (iso-$pO_2$) of the target altitude. METHODS. Literature from investigators and manufacturers indicate that these devices may not properly account for the 47 mmHg of water vapor partial pressure that reduces the inspired partial pressure of $O_2$ ($P_IO_2$). Nor do they account for the complex reality of alveolar gas composition as defined by the Alveolar Gas Equation. In essence, by providing iso-$pO_2$ conditions for normobaric hypoxia (NH) as for HH exposures the devices ignore $P_AO_2$ and $P_ACO_2$ as more direct agents to induce signs and symptoms of hypoxia during acute training exposures. RESULTS. There is not a sufficient integrated physiological understanding of the determinants of $P_AO_2$ and $P_ACO_2$ under acute NH and HH given the same hypoxic $pO_2$ to claim a device that provides isohypoxia. Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic $pO_2$ is an incomplete hypoxic dose. Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m). CONCLUSIONS. At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient $pO_2$ at sea level as at altitude (iso-$pO_2$ machines). An approach to reduce the overestimation is to at least provide machines that create the same $P_IO_2$ (iso-$P_IO_2$ machines) conditions at sea level as at the target altitude, a simple software upgrade.

## INTRODUCTION

Reduced $O_2$ breathing devices create a normobaric hypoxic (NH) exposure by providing an $F_IO_2$ < 0.209, breathed either through a mask or within a "hypoxia tent".

~~The~~ Some manufacturers claim an equivalent acute hypobaric hypoxic (HH) experience but under NH conditions. This eliminates the need for an expensive hypobaric chamber and the risk of decompression sickness associated with hypobaric exposure, creating ~~. So~~ a cost-effective hypoxia training niche ~~is created with these devices, if they~~ these devices deliver ~~what they~~ as promised.

## METHODS

~~We reviewed~~ Literature was reviewed to understand the operations of three reduced $O_2$ breathing devices: ROBD® (1), PROTE® (8), and $GO_2$Altitude® (http://www.hypoxic-training.com).

The devices seem to duplicate the ambient partial pressure of $O_2$ (iso-$pO_2$) at sea level as exists at the target altitude~~, or something else besides $P_IO_2$~~ (7).

The method to convert feet altitude to ambient pressure was never specified, a necessary detail to understand the operation of these devices. ~~But~~ Through analysis, it appears that Eq. 1 is used.

Eq. 1 defines a "Standard Atmosphere - 1976" where distance in kilometers is converted to the equivalent ambient pressure as mmHg.

$$PB_{hypo}\ (mmHg) = 760 * [288.15 / (288.15 - 6.5 * altitude\ (km))]^{-5.25588} \qquad \text{Eq. 1}$$

Eq. 2 is an alternative to Eq. 1 (10).

$$PB_{hypo}\ (mmHg) = \exp[6.63268 - 0.1112 * altitude\ (km) - 0.00149 * altitude^2\ (km)] \qquad \text{Eq. 2}$$

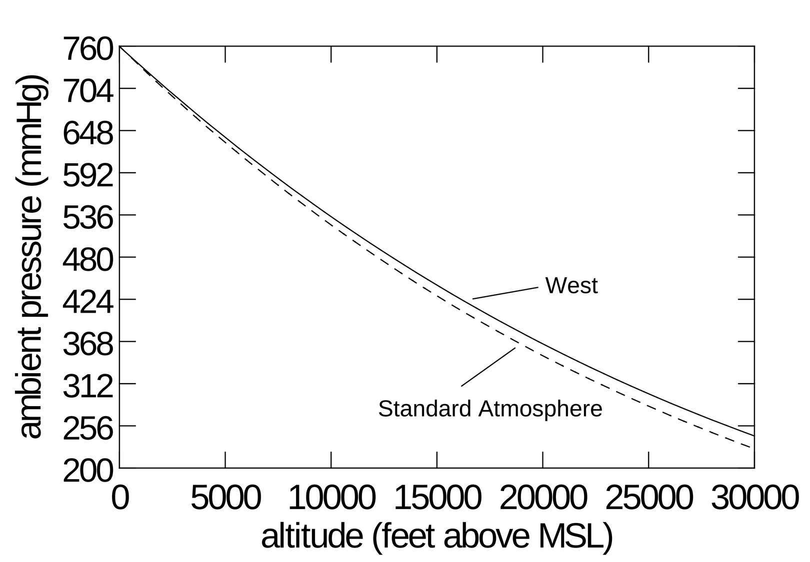


Fig. 1: The relationship between pressure and altitude as feet above mean sea level (MSL) diverges given two equations.

Eq. 3 converts the y-axis in Fig. 1 to $F_IO_2$ under normobaric pressure ($F_IO_{2normo}$) that represents the $pO_2$ while breathing air at these pressures for the iso-$pO_2$ machines (Fig. 2).

$$F_IO_{2normo} = PB_{hypo} * F_IO_{2hypo} / PB_{normo} \qquad \text{Eq. 3}$$

where $PB_{normo}$ is most often 760 mmHg, but could be different if the training is done at a location other than sea level, $F_IO_{2hypo}$ is most often 0.209 but could be different if you are breathing an $O_2$ mixture that is not "air", and $PB_{hypo}$ comes from either Eq. 1 or 2 that computes the ambient pressure for a particular altitude.

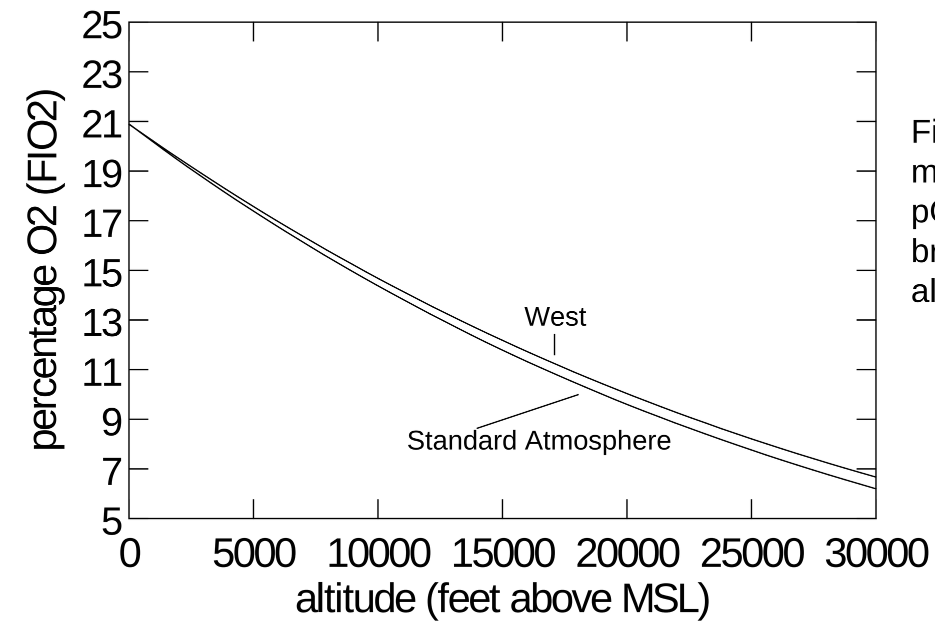


Fig. 2: $F_IO_2$ needed at 760 mmHg to provide the equivalent $pO_2$ you would breathe while breathing air at the given altitude.

Eq. 4 computes the $F_IO_2$ under normobaric conditions ($F_IO_{2normo}$) to provide for iso-$P_IO_2$.

$$F_IO_{2normo} = (PB_{hypo} - 47) * F_IO_{2hypo} / (PB_{normo} - 47) \qquad \text{Eq. 4}$$

This simple improvement would provide a device that delivers a simulation of HH while under NH conditions accounting for 47 mmHg of water vapor pressure, as seen in Fig. 3.

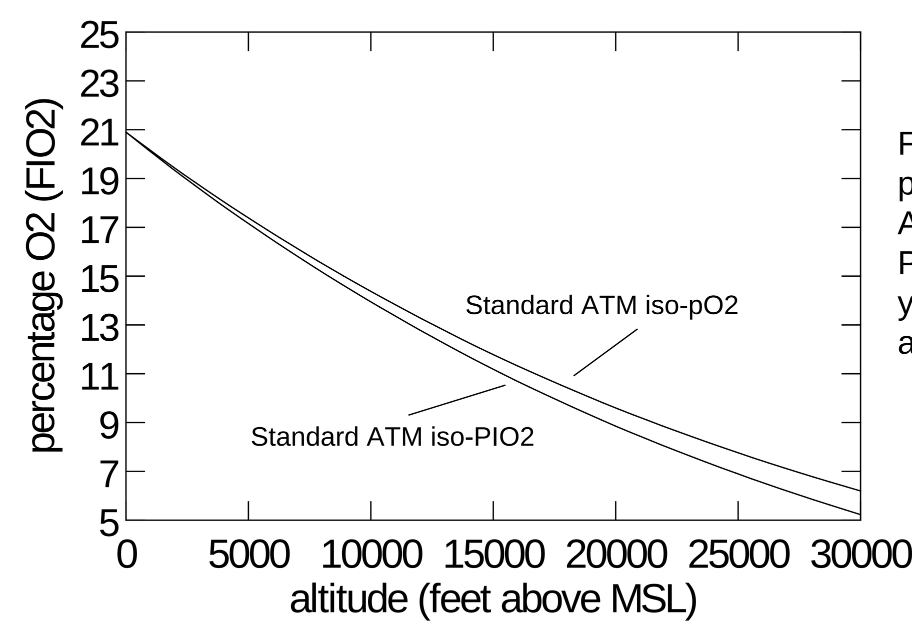


Fig. 3: $F_IO_2$ needed at 760 mmHg to provide the equivalent $pO_2$ (Standard ATM iso-$pO_2$ curve) or the equivalent $P_IO_2$ (Standard ATM iso-$P_IO_2$ curve) you would breathe while breathing air at the given altitude.

The difficulty in using the upper curve in Fig. 3 is that when you provide a $F_IO_2$ at sea level to match the $pO_2$ at the target altitude you create a $P_IO_2$ that is greater than the $P_IO_2$ at the target altitude, a consequence of ignoring $pH_2O$.

It is best to provide a $F_IO_2$ at sea level as defined by the lower curve in Fig. 3 that at least produces the equivalent $P_IO_2$ at sea level as at the target altitude, ~~a consequence of not ignoring~~ which would account for $pH_2O$.

Example: 9.0% $F_IO_2$ at 1 ATA on the display of an iso-$pO_2$ machine would indicate that you are at about 21,500 feet altitude with a $pO_2$ of 68.5 mmHg (Eq. 3). But $P_IO_2$ at 1 ATA is 64.1 mmHg, equivalent to breathing air at 19,700 feet, so an iso-$pO_2$ machine overestimates the simulated altitude by 1,800 feet. This is a consequence of ignoring the contribution of $pH_2O$.

## RESULTS

Even accounting for $pH_2O$ is not sufficient to account for $P_AO_2$ and $P_ACO_2$ as more direct agents to induce signs and symptoms of hypoxia during acute training exposures (2).

Fenn et al., as early as 1946, provided the theoretical foundation on why alveolar gas composition would *never be identical* under NH and HH conditions given the same hypoxic $P_IO_2$, a consequence captured in the derivation of the Alveolar Gas Equation.

Fig. 4 is an example of how NH and HH given the same $P_IO_2$ of 57.3 mmHg (22,000 ft) would not produce identical $P_AO_2$ and $P_ACO_2$.

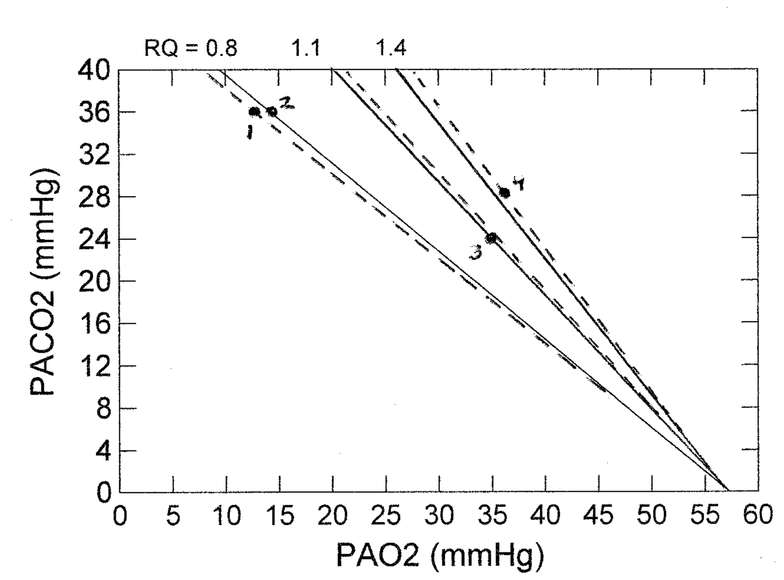


Fig. 4. Application of the Alveolar Gas Equation to demonstrate the inability to accurately reproduce HH under NH conditions given an example of an acute hypobaric training exposure to 22,000 ft. $P_IO_2$ is 57.3 mmHg in both conditions, the intercept for all respiratory quotient (RQ) diagonals when $P_ACO_2$ is zero. Diagonals for HH are solid lines and those for NH (8% $F_IO_2$) are dashed lines, all from the Alveolar Gas Equation (Eq. 5).

$$P_AO_2 = P_IO_2 - P_ACO_2 * [F_IO_2 + ((1 - F_IO_2) / RQ)]. \qquad \text{Eq. 5}$$

Point 1: NH trainee dons mask at 760 mmHg with $F_IO_2$ of 8% and RQ of 0.8, and $P_AO_2$ quickly drops to 13 mmHg – a stimulus to hyperventilate.

Point 2: HH trainee rapidly ascends on air to 22,000 feet with same RQ of 0.8, and $P_AO_2$ quickly drops to about 14 mmHg – a slightly less stimulus to hyperventilate than NH.

Point 3: Hyperventilation of *rarified air* in this example acutely places HH trainee on the 1.1 RQ diagonal given the conditions in Table 1, column 2.

**TABLE 1. Reasonable Response to Acute HH and NH Exposures**

| parameter | HH Example $P_IO_2$ 57 mmHg | NH Example $P_IO_2$ 57 mmHg |
|---|---|---|
| PB (mmHg) | 321 | 760 |
| $F_IO_2$ | 0.21 | 0.08 |
| $V_E$ ($l_{BTPS}$/min) | 14.3 | 16.5 ↑ |
| $V_A$ ($l_{BTPS}$/min) | 10.4 | 12.0 ↑ |
| $VCO_2$($ml_{STPD}$/min) | 289 | 389 ↑ |
| $VO_2$ ($ml_{STPD}$/min) | 262 | 278 ↑ |
| RQ | 1.1 | 1.4 ↑ |
| $V_A/VCO_2$ | 0.036 | 0.031 ↓ |
| $P_AO_2$ mmHg | 35 | 37 ↑ |
| $P_ACO_2$ mmHg | 24 | 28 ↑ |
| $P_AN_2$ (mmHg) | 215 | 648 ↑ |

Point 4: Hyperventilation of *dense air* in this example acutely places NH trainee on the 1.4 RQ diagonal given the conditions in Table 1, column 3.

Loeppky et al. 1997 (and others) shows a greater increase in the rate and depth of breathing in NH relative to HH. In the above example the increase in minute ventilation ($V_E$) and alveolar ventilation ($V_A$) in NH relative to HH results is a greater $P_AO_2$ and $P_ACO_2$ as a result of increased $VCO_2$ from breathing the relatively dense gas during NH.

It follows from Loeppky and our example in Fig. 4 that physiological responses would be different after peripheral and central chemoreceptor responses are integrated within the central nervous system.

Even if the Alveolar Gas Equation was used in reduced $O_2$ breathing devices one must account for the complex time-dependent role that $P_AN_2$ has in modifying $P_AO_2$ and $P_ACO_2$ under a particular hypoxic $P_IO_2$.

An accurate application of the Alveolar Gas Equation requires that the inspired $N_2$ volume be equal to the expired $N_2$ volume:

$$VN_2 = V_I * F_IN_2 - V_E * F_EN_2 = 0. \qquad \text{Eq. 6}$$

Eq. 6 is applicable in maneuvers such as breath holding, voluntary hyperventilation, or exercise. But Eq. 6 is invalid to greater or lesser degree when ambient pressure changes or $F_IO_2 \neq 0.209$, or some combination of both *until* a new $P_AN_2$ equilibrium is established.

NH necessarily requires $N_2$ molecules to move from the lungs into the tissues while HH requires $N_2$ molecules to move from the tissues into the lungs, each moving under different concentration gradients and possibly different time constants until a new dynamic equilibrium is achieved during a chronic NH or HH exposure.

The transient movement of $N_2$ changes $P_AN_2$ at constant PB, so changes the $O_2$-$CO_2$ point between NH and HH until the differences eventually become small and constant as each $O_2$-$CO_2$ point migrates onto its appropriate RQ diagonal near 0.8.

## CONCLUSIONS

**TABLE 2. Unresolved Issues Given Same Hypoxic $P_IO_2$**

| parameter | HH | NH | acute➔*time*➔chronic |
|---|---|---|---|
| $f_v$ | ↓ | ↑ | ? |
| $V_T$ | ↓ | ↑ | ? |
| $V_E$ | ↓ | ↑ | ? |
| $V_A$ | ↓ | ↑ | ? |
| $VCO_2$ | ↓ | ↑ | ? |
| $VO_2$ | ↓ | ↑ | ? |
| RQ | ↓ | ↑ | ? |
| $V_A/VCO_2$ | ↑ | ↓ | ? |
| $P_AO_2$ | ↓ | ↑ | ? |
| $P_ACO_2$ | ↓ | ↑ | ? |
| $F_EN_2/F_IN_2$ | ↑ | ↓ | ? |
| $V_D/V_T$ | ? | ? | ? |
| Q | ? | ? | ? |
| $V_A/Q$ | ↑ (5) | ? | ? |
| $pH_{CSF}$ | ? | ? | ? |
| % AMS | ↑ | ↓ | ? |

There is not an adequate integrated physiological understanding of the determinants of $P_AO_2$ and $P_ACO_2$ under NH and HH given the same hypoxic $pO_2$ to claim a device that provides TRUE isohypoxia.

Isohypoxia is defined as the same distribution of hypoxia signs and symptoms under any circumstances of equivalent hypoxic dose, and hypoxic $pO_2$ or even $P_IO_2$ are incomplete doses (3).

*Both* time-dependent $P_AO_2$ and $P_ACO_2$ should be considered in a calculation of hypoxic dose.

We *hypothesize* that the integrated hypoxic dose over the same exposure time is less in NH than HH for the same hypoxic $P_IO_2$.

Some devices that claim an equivalent HH experience under NH conditions significantly overestimate the HH condition, especially when simulating altitudes above 10,000 feet (3,048 m).

At best, the claim should be that the devices provide an *approximate* HH experience since they only duplicate the ambient $pO_2$ at sea level as at altitude (iso-$pO_2$ machines).

A first step ~~n~~ approach to reduce the overestimation is to at least provide machines that create the same $P_IO_2$ (iso-$P_IO_2$ machines) conditions at sea level as at the target altitude, a simple software upgrade from Eq. 3 to Eq. 4.

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